

## PATENT ABSTRACTS OF JAPAN

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A61P 3/10  
A61P 9/10  
A61P 17/06  
A61P 19/02  
A61P 27/02  
A61P 29/00  
A61P 35/00  
C07D413/12  
C07D417/12

(21)Application number : 2002-126869

(71)Applicant : KIRIN BREWERY CO LTD

(22)Date of filing : 26.04.2002

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ISOE TOSHIYUKI  
HASEGAWA KAZUMASA

(30)Priority

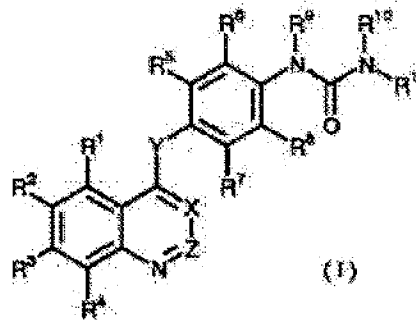
Priority number : 2001132775 Priority date : 27.04.2001 Priority country : JP

### (54) QUINOLIN DERIVATIVE HAVING AZOLYL GROUP AND QUINAZOLIN DERIVATIVE

(57)Abstract:

PROBLEM TO BE SOLVED: To provide a compound having strong antitumor activities.

SOLUTION: This compound is the one represented by formula (I) (wherein, X and Z are each CH or N; Y is O or S; R1, R2, and R3 are each H, an alkoxy or the like; R4 is H; R5, R6, R7 and R8 are each H, a halogen, an alkoxy, or the like; R9 and R10 are each H, an alkyl, or the like; R11 is an azolyl which may be substituted), or a pharmaceutically acceptable salt or solvate thereof.



(I)

(19) 日本国特許庁 (J P)

(12) 公開特許公報 (A)

(11) 特許出願公開番号

特開2003-12668

(P2003-12668A)

(43) 公開日 平成15年1月15日 (2003.1.15)

(51) Int.Cl. <sup>7</sup>	識別記号	F I	テ-マ-ト*(参考)
C 0 7 D 401/12		C 0 7 D 401/12	4 C 0 6 3
A 6 1 K 31/4709		A 6 1 K 31/4709	4 C 0 8 6
	31/517	31/517	
A 6 1 P 3/10		A 6 1 P 3/10	
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(21) 出願番号 特願2002-126869(P2002-126869)

(22) 出願日 平成14年4月26日 (2002.4.26)

(31) 優先権主張番号 特願2001-132775(P2001-132775)

(32) 優先日 平成13年4月27日 (2001.4.27)

(33) 優先権主張国 日本 (J P)

(71) 出願人 000253503

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東京都中央区新川二丁目10番1号

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居寮207号

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群馬県高崎市宮原町11 宮原社宅A-204

(74) 代理人 100075812

弁理士 吉武 賢次 (外3名)

最終頁に続く

(54) 【発明の名称】 アゾリル基を有するキノリン誘導体およびキナゾリン誘導体

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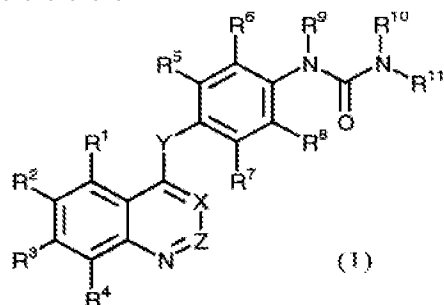
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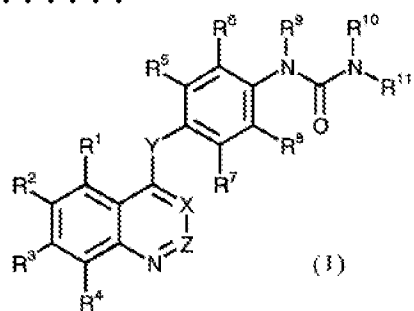
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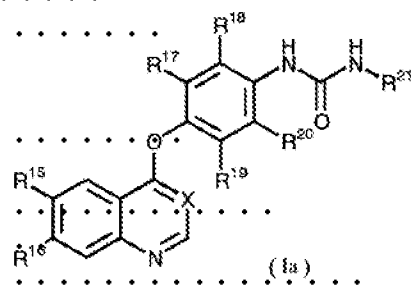
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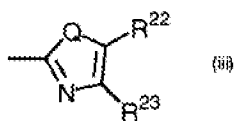
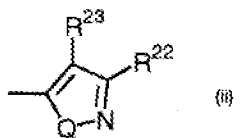
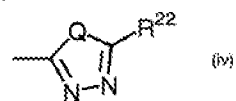
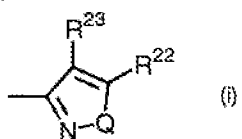


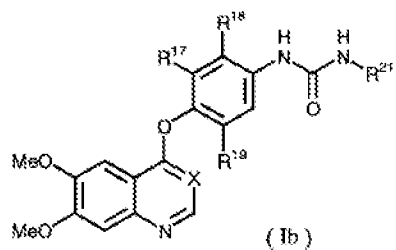
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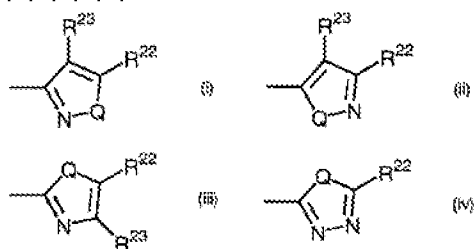
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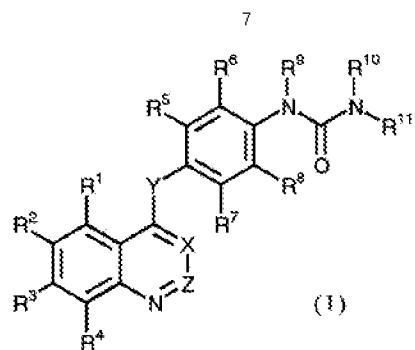
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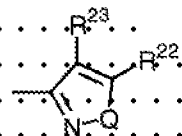
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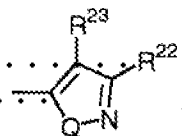
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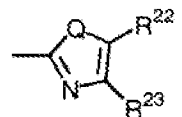
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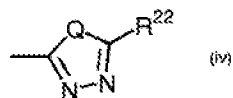
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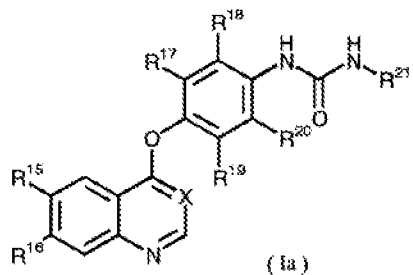
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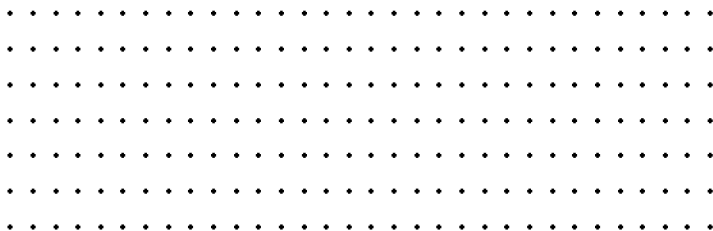


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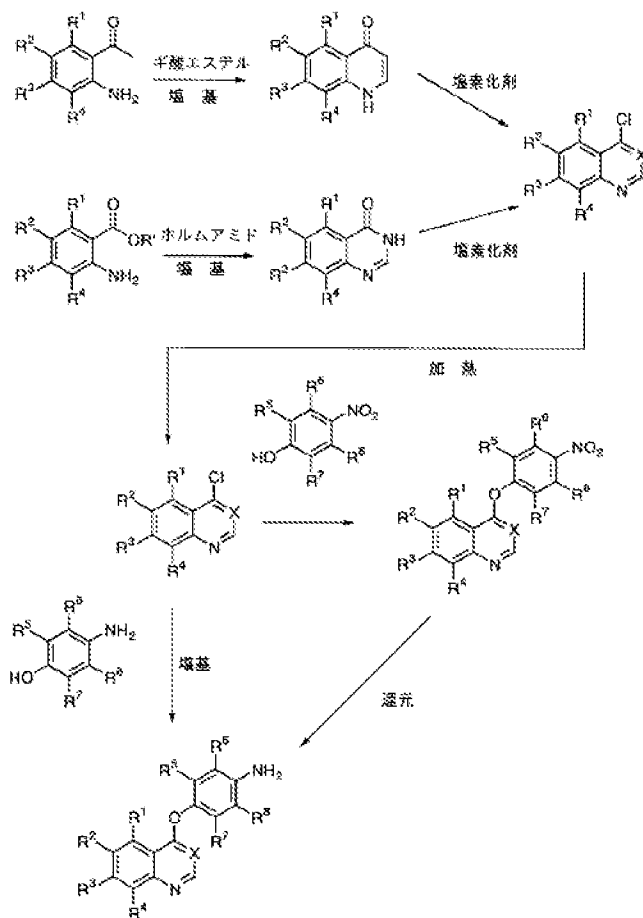
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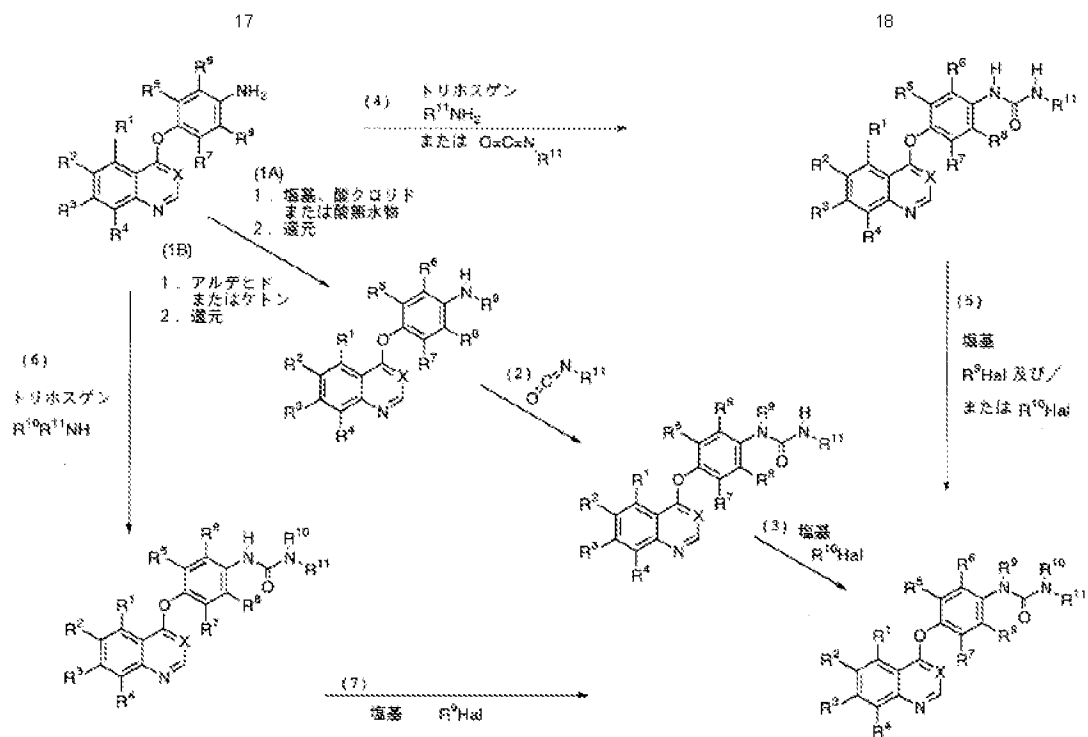


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This image shows a full page of dot grid paper. The dots are arranged in a precise, repeating pattern across the entire surface, forming a grid that is useful for writing, drawing, or organizing information. The dots are small and dark, set against a light background.

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Date: _____	
Page: _____	
1. _____	_____
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This image shows a full page of dot grid paper. The background is white, and it is covered with a uniform grid of small black dots. The dots are arranged in straight horizontal and vertical lines, creating a precise grid pattern across the entire surface. There are no margins, text, or other markings present.

[illegible]

Date: _____		Page: _____	
<p>1. _____</p> <p>2. _____</p> <p>3. _____</p> <p>4. _____</p> <p>5. _____</p> <p>6. _____</p> <p>7. _____</p> <p>8. _____</p> <p>9. _____</p> <p>10. _____</p> <p>11. _____</p> <p>12. _____</p> <p>13. _____</p> <p>14. _____</p> <p>15. _____</p> <p>16. _____</p> <p>17. _____</p> <p>18. _____</p> <p>19. _____</p> <p>20. _____</p> <p>21. _____</p> <p>22. _____</p> <p>23. _____</p> <p>24. _____</p> <p>25. _____</p> <p>26. _____</p> <p>27. _____</p> <p>28. _____</p> <p>29. _____</p> <p>30. _____</p> <p>31. _____</p> <p>32. _____</p> <p>33. _____</p> <p>34. _____</p> <p>35. _____</p> <p>36. _____</p> <p>37. _____</p> <p>38. _____</p> <p>39. _____</p> <p>40. _____</p> <p>41. _____</p> <p>42. _____</p> <p>43. _____</p> <p>44. _____</p> <p>45. _____</p> <p>46. _____</p> <p>47. _____</p> <p>48. _____</p> <p>49. _____</p> <p>50. _____</p>		<p>1. _____</p> <p>2. _____</p> <p>3. _____</p> <p>4. _____</p> <p>5. _____</p> <p>6. _____</p> <p>7. _____</p> <p>8. _____</p> <p>9. _____</p> <p>10. _____</p> <p>11. _____</p> <p>12. _____</p> <p>13. _____</p> <p>14. _____</p> <p>15. _____</p> <p>16. _____</p> <p>17. _____</p> <p>18. _____</p> <p>19. _____</p> <p>20. _____</p> <p>21. _____</p> <p>22. _____</p> <p>23. _____</p> <p>24. _____</p> <p>25. _____</p> <p>26. _____</p> <p>27. _____</p> <p>28. _____</p> <p>29. _____</p> <p>30. _____</p> <p>31. _____</p> <p>32. _____</p> <p>33. _____</p> <p>34. _____</p> <p>35. _____</p> <p>36. _____</p> <p>37. _____</p> <p>38. _____</p> <p>39. _____</p> <p>40. _____</p> <p>41. _____</p> <p>42. _____</p> <p>43. _____</p> <p>44. _____</p> <p>45. _____</p> <p>46. _____</p> <p>47. _____</p> <p>48. _____</p> <p>49. _____</p> <p>50. _____</p>	

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This image shows a full page of dot grid paper. The background is a solid light gray color. Overlaid on this background is a precise grid of small, dark gray dots. The dots are arranged in perfectly straight horizontal and vertical rows, creating a series of small squares across the entire page. There are no margins, text, or other markings present.

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Time	Activity
0:00	Start of the day
0:10	First break
0:20	Second break
0:30	Third break
0:40	Fourth break
0:50	Fifth break
1:00	Sixth break
1:10	Seventh break
1:20	Eighth break
1:30	Ninth break
1:40	Tenth break
1:50	Eleventh break
2:00	Twelfth break
2:10	Thirteenth break
2:20	Fourteenth break
2:30	Fifteenth break
2:40	Sixteenth break
2:50	Seventeenth break
3:00	Eighteenth break
3:10	Nineteenth break
3:20	Twentieth break
3:30	Twenty-first break
3:40	Twenty-second break
3:50	Twenty-third break
4:00	Twenty-fourth break
4:10	Twenty-fifth break
4:20	Twenty-sixth break
4:30	Twenty-seventh break
4:40	Twenty-eighth break
4:50	Twenty-ninth break
5:00	Thirtieth break
5:10	Thirty-first break
5:20	Thirty-second break
5:30	Thirty-third break
5:40	Thirty-fourth break
5:50	Thirty-fifth break
6:00	Thirty-sixth break
6:10	Thirty-seventh break
6:20	Thirty-eighth break
6:30	Thirty-ninth break
6:40	Fortieth break
6:50	Forty-first break
7:00	Forty-second break
7:10	Forty-third break
7:20	Forty-fourth break
7:30	Forty-fifth break
7:40	Forty-sixth break
7:50	Forty-seventh break
8:00	Forty-eighth break
8:10	Forty-ninth break
8:20	Fiftieth break
8:30	Fifty-first break
8:40	Fifty-second break
8:50	Fifty-third break
9:00	Fifty-fourth break
9:10	Fifty-fifth break
9:20	Fifty-sixth break
9:30	Fifty-seventh break
9:40	Fifty-eighth break
9:50	Fifty-ninth break
10:00	Sixtieth break
10:10	Sixty-first break
10:20	Sixty-second break
10:30	Sixty-third break
10:40	Sixty-fourth break
10:50	Sixty-fifth break
11:00	Sixty-sixth break
11:10	Sixty-seventh break
11:20	Sixty-eighth break
11:30	Sixty-ninth break
11:40	Seventieth break
11:50	Seventy-first break
12:00	Seventy-second break
12:10	Seventy-third break
12:20	Seventy-fourth break
12:30	Seventy-fifth break
12:40	Seventy-sixth break
12:50	Seventy-seventh break
13:00	Seventy-eighth break
13:10	Seventy-ninth break
13:20	Eightieth break
13:30	Eighty-first break
13:40	Eighty-second break
13:50	Eighty-third break
14:00	Eighty-fourth break
14:10	Eighty-fifth break
14:20	Eighty-sixth break
14:30	Eighty-seventh break
14:40	Eighty-eighth break
14:50	Eighty-ninth break
15:00	Ninetieth break
15:10	Ninety-first break
15:20	Ninety-second break
15:30	Ninety-third break
15:40	Ninety-fourth break
15:50	Ninety-fifth break
16:00	Ninety-sixth break
16:10	Ninety-seventh break
16:20	Ninety-eighth break
16:30	Ninety-ninth break
16:40	Hundredth break

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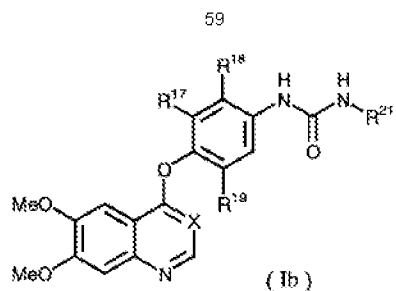
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実施例	X	R <sup>17</sup>	R <sup>18</sup>	R <sup>19</sup>	R <sup>21</sup>	G	R <sup>22</sup>	R <sup>23</sup>
1	CH	Cl	H	H	(1)	O	H	H
2	CH	Cl	H	H	(11)	O	CH <sub>3</sub>	H
3	CH	F	H	H	(1)	O	H	H
4	CH	H	Cl	H	(1)	O	CH <sub>3</sub>	H
5	CH	H	Cl	H	(11)	O	CH <sub>3</sub>	H
6	CH	H	F	H	(11)	O	CH <sub>3</sub>	H
7	CH	F	H	H	(11)	O	CH <sub>3</sub>	H
8	CH	F	H	H	(1)	O	CH <sub>3</sub>	H
9	CH	H	F	H	(1)	O	CH <sub>3</sub>	H
10	N	H	H	H	(1)	O	CH <sub>3</sub>	H
11	N	H	H	H	(11)	O	CH <sub>3</sub>	H
12	N	H	Cl	H	(1)	O	CH <sub>3</sub>	H
13	N	H	Cl	H	(11)	O	CH <sub>3</sub>	H
14	N	Cl	H	H	(1)	O	CH <sub>3</sub>	H
15	N	Cl	H	H	(11)	O	CH <sub>3</sub>	H
16	N	H	H	H	(11)	S	CH <sub>3</sub>	H
17	N	H	Cl	H	(11)	S	CH <sub>3</sub>	H
18	N	Cl	H	H	(11)	S	CH <sub>3</sub>	H
19	CH	Cl	H	H	(11)	NH	H	H
20	CH	H	F	H	(11)	NH	H	H
21	CH	H	F	H	(111)	S	CH <sub>3</sub>	H
22	CH	H	Cl	H	(111)	S	H	CH <sub>3</sub>
23	CH	H	F	H	(111)	S	CH <sub>3</sub>	CH <sub>3</sub>
24	CH	H	Cl	H	(111)	S	CH <sub>3</sub>	CH <sub>3</sub>
25	CH	Cl	H	H	(111)	S	CH <sub>3</sub>	CH <sub>3</sub>
26	CH	H	CF <sub>3</sub>	H	(111)	S	CH <sub>3</sub>	CH <sub>3</sub>
27	CH	H	F	H	(111)	S	H	H
28	CH	H	F	H	(111)	S	H	CH <sub>3</sub>
29	CH	H	F	H	(111)	S	H	A
30	CH	H	F	H	(111)	S	H	tBu
31	CH	H	Cl	H	(111)	S	H	A
32	CH	H	Cl	H	(111)	S	Br	H
33	CH	H	Cl	H	(111)	S	H	tBu
34	CH	H	Cl	H	(111)	S	Cl	H



35	CH	H	F	H	(iii)	S	Br	H
36	CH	H	F	H	(iii)	S	Ac	CH <sub>3</sub>
37	CH	H	F	H	(iii)	S	Cl	H
38	N	H	Cl	H	(iii)	S	H	H
39	N	H	Cl	H	(iii)	S	CH <sub>3</sub>	H
40	N	H	Cl	H	(iii)	S	CH <sub>3</sub>	CH <sub>3</sub>
41	N	H	Cl	H	(iii)	S	H	CH <sub>3</sub>
42	N	H	H	H	(iii)	S	H	H
43	N	H	H	H	(iii)	S	CH <sub>3</sub>	H
44	N	H	H	H	(iii)	S	H	CH <sub>3</sub>
45	N	H	H	H	(iii)	S	CH <sub>3</sub>	CH <sub>3</sub>
46	N	Cl	H	H	(iii)	S	H	H
47	N	Cl	H	H	(iii)	S	CH <sub>3</sub>	H
48	N	Cl	H	H	(iii)	S	H	CH <sub>3</sub>
49	N	Cl	H	H	(iii)	S	CH <sub>3</sub>	CH <sub>3</sub>
50	CH	H	H	H	(iv)	S	CF <sub>3</sub>	H
51	CH	H	F	H	(iv)	S	CF <sub>3</sub>	H
52	CH	F	H	H	(iv)	S	CF <sub>3</sub>	H
53	CH	CH <sub>3</sub>	CH <sub>3</sub>	H	(iv)	S	CF <sub>3</sub>	H
54	CH	H	H	H	(iv)	S	CH <sub>3</sub>	H
55	CH	H	CH <sub>3</sub>	H	(iv)	S	CH <sub>3</sub>	H
56	CH	CH <sub>3</sub>	H	H	(iv)	S	CH <sub>3</sub>	H
57	CH	CH <sub>3</sub>	CH <sub>3</sub>	H	(iv)	S	CH <sub>3</sub>	H
58	CH	H	F	H	(iv)	S	CH <sub>3</sub>	H
59	CH	H	H	H	(iv)	S	Et	H
60	CH	H	CH <sub>3</sub>	H	(iv)	S	Et	H
61	CH	CH <sub>3</sub>	H	H	(iv)	S	Et	H
62	CH	CH <sub>3</sub>	CH <sub>3</sub>	H	(iv)	S	Et	H
63	CH	H	F	H	(iv)	S	Et	H
64	CH	F	H	H	(iv)	S	Et	H
65	CH	H	Cl	H	(iv)	S	Et	H
66	CH	Cl	H	H	(iv)	S	Et	H
67	CH	H	Cl	H	(iv)	S	cPr	H
68	CH	Cl	H	H	(iv)	S	cPr	H
69	CH	H	CH <sub>3</sub>	CH <sub>3</sub>	(iv)	S	cPr	H

70	CH	H	F	H	(iv)	S	EtS	H
71	CH	CH <sub>3</sub>	CH <sub>3</sub>	H	(iv)	S	EtS	H
72	CH	H	Cl	H	(iv)	S	CF <sub>3</sub>	H
73	CH	Cl	H	H	(iv)	S	CF <sub>3</sub>	H
74	CH	H	F	H	(iv)	S	EtU	H
75	CH	CH <sub>3</sub>	CH <sub>3</sub>	H	(iv)	S	EtU	H

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2040

	TGIR (%)
实施例 3	39.5
实施例 4	55.4
实施例 5	29.5
实施例 6	29.3
实施例 9	63.5
实施例 21	66.6
实施例 22	43.8
实施例 23	51.7
实施例 24	39.8
实施例 25	18.8
实施例 28	66.3
实施例 29	66.1
实施例 38	92.0
实施例 39	64.0
实施例 40	34.2
实施例 50	11.9
实施例 51	45.6
实施例 52	20.7
实施例 53	14.4
实施例 58	13.4
实施例 69	23.3

化合物	投与用量 (mg/kg)	TGIR (%)
4	0.2	62
4	0.5	80
4	1	88
27	5	82
28	5	59
38	5	78

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癌細胞	投与用量 (mg/kg)	TGIR (%)
LS174T	5	65
A549	20	65